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# Structure of Pex5p and Pex5-20 complexes in the yeast *Hansenula polymorpha*. Pex20p causes a conformational change upon binding to Pex5p tetramers involved in peroxisomal protein transport.

Kasia Moscicka<sup>1</sup>, Sandra H. Klompmaker<sup>2</sup>, Dongyuan Wang<sup>2</sup>, Ida J. van der Klei<sup>2</sup>  
and Egbert J. Boekema<sup>1</sup>

1. Electron Microscopy, and <sup>b</sup>Eukaryotic Microbiology, Groningen Biomolecular  
Sciences and Biotechnology Institute (GBB), University of Groningen, <sup>a</sup>Nijenborgh 4,  
9747 AG Groningen, The Netherlands  
2. Kerklaan 30, 9751 NN Haren, The Netherlands

K.B.Moscicka@rug.nl

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Peroxisomal matrix proteins are synthesized on free polyribosomes and directed to the organelle by specific peroxisomal targeting signals (PTSs).

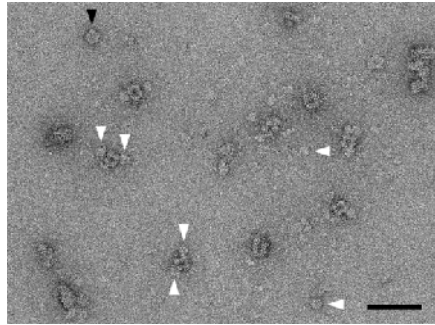
The *PEX5* gene encodes the PTS1 receptor, Pex5p, which interacts with the PTS1 signal via a series of tetratricopeptide repeats (TPRs) within its C terminus. A crystal structure has been determined of a 41 kDa fragment of human Pex5p that includes six TPR motifs in complex with a small peptide containing a PTS1 sequence [1,2] or the sterol carrier protein [3]. This structure reveals the molecular basis for PTS1 recognition which is mostly formed by two clusters of three TPRs almost completely surrounding the PTS1-peptide.

However, whether or not Pex5p functions as an oligomer, is still a matter of debate. Gel filtration chromatography and electron microscopy studies indicated that human Pex5p (HsPex5p) is a homotetramer [4]. Fluorescence spectroscopy studies on Pex5p of the yeast *Hansenula polymorpha* (HpPex5p) indicated that HpPex5p also forms oligomers [5].

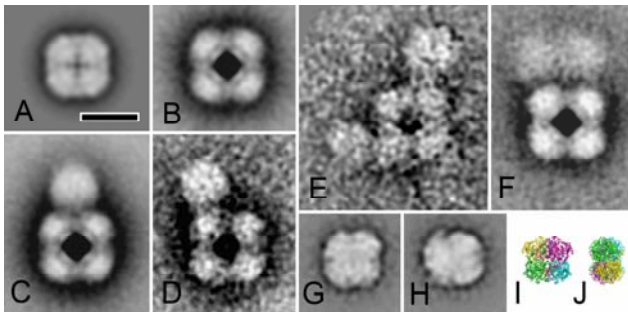
In this study, the projection structures of HpPex5p and HpPex5p-HpPex20p complexes were investigated by single particle electron microscopy. The analysis shows that HpPex5p is a tetramer and that HpPex20p is able to induce a major conformational change leading to a rather open space in the centre of the HpPex5p tetramer. In a successive set of experiments we show that HpPex5p-HpPex20p complexes are able to bind folded copies of tetrameric catalase at the periphery. Since catalase is one of the major peroxisomal proteins this indicates that such HpPex5p-HpPex20p-catalase complexes are functional as receptor complex.

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**Figure 1.** Electron micrograph of negatively stained Pex5p-20p complexes. The black arrowhead points to a Pex5p tetramer in the closed conformation; the white arrowheads indicate Pex20, either attached to Pex5p in the open conformation or as single complexes. The space bar indicates 50 nm.



**Figure 2.** Single particle image analysis of Pex5p, Pex5-20 and Pex5-20-catalase complexes. (A) Average projection map of purified Pex5p in the closed conformation. (B) Average projection map of purified Pex5p in the open conformation. (C) main view of the Pex5-20 complex. (D) average map of a small class of Pex5-20 complexes in which the upper Pex20 multimer is displaced. (E). Another class of Pex5-20 complexes in which a Pex20 multimer second multimer is binding to the left side of the Pex5p tetramer. (F) main class of Pex5-20-catalase complexes (G,H) main views of purified catalase tetramers. (I) High-resolution catalase X-ray model in a position similar to the EM projection of image G, in which it is slightly tilted out of its 4-fold symmetrical view. (H) side-view of the X-ray model in which two monomers are almost in overlap with two others. Four-fold symmetry was imposed on images of (A) and (B) after completion of analysis. The space bar equals 10 nm.